

Appendix: Supplementary tables A-C [posted as supplied by author]

Table A. Hazard ratio (HR) and 95% confidence interval for asthma *drugs* and *diagnosis* separately, in relation to exposure to antibiotics in fetal life, in the full cohort of children and for children with siblings.

	All children [¤]		Children with siblings			
	Crude [†]	Adjusted ^{‡*}	Crude		Adjusted*	
Group of antibiotics	HR (95% CI)	HR (95% CI)	Cases ^º	HR (95% CI)	Cases	HR (95% CI)
Asthma drugs						
Any	1.33 (1.30 to 1.36)	1.27 (1.24 to 1.30)	3 983	0.99 (0.93 to 1.05)	3 589	1.00(0.94 to 1.06)
Airway	1.41 (1.37 to 1.44)	1.32 (1.28 to 1.35)	2 818	0.99 (0.92 to 1.06)	2 546	1.00 (0.93 to 1.08)
Urinary tract/Skin	1.20 (1.16 to 1.23)	1.18 (1.15 to 1.22)	1 678	0.96 (0.88 to 1.05)	1 498	0.96 (0.87 to 1.05)
Asthma diagnosis						
Any	1.32 (1.29 to 1.35)	1.25 (1.22 to 1.28)	3 702	1.01 (0.95 to 1.07)	3 353	1.02 (0.95 to 1.08)
Airway	1.37 (1.34 to 1.41)	1.27 (1.24 to 1.31)	2 592	0.99 (0.93 to 1.07)	2 338	0.99 (0.92 to 1.07)
Urinary tract/Skin	1.22 (1.19 to 1.26)	1.20 (1.16 to 1.24)	1 592	1.03 (0.94 to 1.13)	1 443	1.05 (0.95 to 1.15)

[¤] Children to mothers with prescriptions of antibiotics without license in Sweden during the study period (n=9) were excluded.

* Adjusted for maternal smoking during pregnancy, parity, family situation (cohort and sibling analyses) and mother's birth country, parental education, maternal asthma (cohort analyses), and age as analysis time scale. Individuals with missing information on included variables excluded. ^ºCases - number of families with siblings discordant for both antibiotic exposure and asthma.

Asthma drugs

[†] 23 100 000 Person years and 44 823 events; individuals with reported event before date of entry (birth) were excluded (n=14)

[‡] 22 000 000 Person years and 42 144 events.

Asthma diagnosis

[†] 23 200 000 Person years and 41 780 events; individuals with reported event before date of entry (birth) were excluded (n=1)

[‡] 22 000 000 Person years and 39 414 events.

Table B. Hazard ratio (HR) and 95% confidence interval for *asthma drugs* in relation to age at exposure antibiotics in childhood, in the full cohort of children and for children with siblings.

All children							Children with siblings				
Group of antibiotics	1000 PY	Crude		1000 PY	Adjusted*		Cases ^o	Crude		Adjusted**	
		Event	HR (95% CI)		Event	HR (95% CI)		HR (95% CI)	Cases	HR (95% CI)	
Any											
0-0.5 years	245	6 315	4.37 (4.08 to 4.68)	233	5 951	4.21 (3.93 to 4.53)	1 289	2.03 (1.64 to 2.50)	1 128	2.32 (1.84 to 2.94)	
0.5-1	239	12 581	2.93 (2.82 to 3.05)	227	11 859	2.83 (2.72 to 2.94)	2 271	1.69 (1.52 to 1.88)	2 038	1.62 (1.45 to 1.81)	
1-1.5	221	9 649	2.46 (2.36 to 2.56)	210	9 108	2.38 (2.28 to 2.48)	1 339	1.80 (1.59 to 2.03)	1 240	1.76 (1.54 to 2.01)	
1.5-2	189	7 561	2.27 (2.16 to 2.38)	179	7 138	2.19 (2.09 to 2.30)	847	1.55 (1.32 to 1.84)	881	1.58 (1.32 to 1.89)	
2-	632	8 717	2.04 (1.94 to 2.14)	591	8 127	1.97 (1.87 to 2.08)	1 029	1.46 (1.16 to 1.81)	1 102	1.39 (1.09 to 1.76)	
HR (95% CI)			HR (95% CI)				Cases	HR (95% CI)	Cases	HR (95% CI)	
Airway											
0-0.5 years			4.95 (4.60 to 5.31)			4.73 (4.39 to 5.09)	1 238	2.31 (1.85 to 2.88)	1 101	2.68 (2.09 to 3.43)	
0.5-1			3.04 (2.93 to 3.16)			2.90 (2.79 to 3.02)	2 194	1.72 (1.54 to 1.91)	1 984	1.65 (1.47 to 1.85)	
1-1.5			2.51 (2.41 to 2.61)			2.40 (2.31 to 2.51)	1 315	1.82 (1.61 to 2.06)	1 192	1.81 (1.58 to 2.07)	
1.5-2			2.30 (2.19 to 2.41)			2.21 (2.10 to 2.32)	853	1.62(1.37 to 1.92)	786	1.64 (1.37 to 1.96)	
2-			2.05(1.95 to 2.16)			1.97 (1.87 to 2.07)	1 074	1.44 (1.16 to 1.79)	977	1.38 (1.09 to 1.74)	
Urinary tract/Skin											
0-0.5 years			1.76 (1.47 to 2.10)			1.68 (1.40 to 2.02)	137	0.94 (0.59 to 1.51)	125	1.05 (0.63 to 1.77)	
0.5-1			1.62 (1.48 to 1.78)			1.57 (1.43 to 1.73)	329	0.99 (0.78 to 1.25)	294	1.03 (0.80 to 1.32)	
1-1.5			1.43 (1.31 to 1.56)			1.41 (1.30 to 1.54)	310	1.11 (0.87 to 1.42)	284	1.09 (0.84 to 1.41)	
1.5-2			1.27 (1.67 to 1.38)			1.26 (1.16 to 1.38)	300	0.98 (0.75 to 1.27)	275	0.97 (0.73 to 1.30)	
2-			1.28 (1.20 to 1.36)			1.28 (1.20 to 1.37)	503	0.98 (0.73 to 1.31)	448	0.99 (0.72 to 1.36)	

PY – Person years; *Adjusted for sex, birth weight, gestational age, mode of delivery, respiratory diagnoses as newborn, maternal age at delivery, parity, family situation (cohort and sibling analyses), mother's birth country, parental education (cohort analyses), and age as analysis time scale. Individuals with reported event before date of entry (birth) were excluded (n=318). Individuals with missing information on included variables excluded. ** As in (*), but with parity included as an interaction term with age.

^o Cases - Number of families with siblings discordant for both antibiotic exposure and asthma.

Table C. Hazard Ratio (HR) and 95% confidence interval for *asthma diagnosis* in relation to age at exposure to antibiotics in childhood, in the full cohort of children and for children with siblings.

Group of antibiotics	Cohort						Children with siblings			
	Crude			Adjusted*			Crude		Adjusted**	
	1000 PY	Event	HR (95% CI)	1000 PY	Event	HR (95% CI)	Cases ^o	HR (95% CI)	Cases	HR (95% CI)
Any										
0-0.5 years	246	4 677	3.88 (3.56 to 4.22)	233	4 422	3.67 (3.37 to 4.00)	905	1.78 (1.39 to 2.27)	795	1.71 (1.30 to 2.24)
0.5-1	241	9 856	2.97 (2.84 to 3.10)	229	9 323	2.82 (2.70 to 2.95)	1 772	1.70 (1.52 to 1.91)	1 608	1.70 (1.50 to 1.93)
1-1.5	224	8 640	2.48 (2.38 to 2.59)	212	8 172	2.37 (2.64 to 2.47)	1 351	1.88 (1.67 to 2.13)	1 237	1.88 (1.64 to 2.14)
1.5-2	192	7 272	2.36 (2.24 to 2.48)	182	6 908	2.27 (2.16 to 2.39)	952	1.62 (1.37 to 1.92)	852	1.61 (1.34 to 1.93)
2-	643	11 335	2.11 (2.02 to 2.21)	601	10 628	2.03 (1.93 to 2.12)	1 511	1.46 (1.21 to 1.75)	1 394	1.40 (1.14 to 1.70)
			HR (95% CI)			HR (95% CI)	Cases	HR (95% CI)	Cases	HR (95% CI)
Airway										
0-0.5 years		4.42 (4.05 to 4.82)			4.13 (3.78 to 4.52)		874	1.97 (1.52 to 2.56)	771	1.87 (1.41 to 2.49)
0.5-1		3.11 (2.98 to 3.25)			2.93 (2.80 to 3.06)		1 707	1.78 (1.58 to 2.01)	1 534	1.78 (1.56 to 2.02)
1-1.5		2.55 (2.44 to 2.66)			2.41 (2.31 to 2.52)		1 303	1.96 (1.73 to 2.22)	1 176	1.95 (1.71 to 2.23)
1.5-2		2.39 (2.27 to 2.51)			2.29 (2.17 to 2.41)		928	1.61 (1.37 to 1.90)	830	1.60 (1.33 to 1.92)
2-		2.13 (2.04 to 2.23)			2.02 (1.93 to 2.12)		1 499	1.50 (1.25 to 1.80)	1 371	1.42 (1.17 to 1.73)
Urinary tract/Skin										
0-0.5 years		1.47 (1.17 to 1.85)			1.39 (1.10 to 1.76)		92	0.69 (0.39 to 1.25)	83	0.62 (0.33 to 1.19)
0.5-1		1.61 (1.45 to 1.78)			1.54 (1.39 to 1.72)		270	0.98 (0.76 to 1.26)	241	1.00 (0.75 to 1.32)
1-1.5		1.44 (1.32 to 1.57)			1.42 (1.30 to 1.56)		316	0.97 (0.77 to 1.23)	285	1.00 (0.78 to 1.27)
1.5-2		1.36 (1.25 to 1.47)			1.35 (1.24 to 1.47)		293	0.88 (0.68 to 1.15)	264	0.96 (0.72 to 1.27)
2-		1.34 (1.27 to 1.41)			1.34 (1.27 to 1.42)		647	1.39 (1.10 to 1.77)	582	1.42 (1.09 to 1.83)

PY – Person years; *Adjusted for sex, birth weight, gestational age, mode of delivery, respiratory diagnoses as newborn, maternal age at delivery, parity, family situation (cohort and sibling analyses), mother's birth country, parental education (cohort analyses), and age as analysis time scale. Individuals with reported event before date of entry (birth) were excluded (n=305). Individuals with missing information on included variables excluded. ** As in (*), but with parity included as an interaction term with age.

^o Cases - Number of families with siblings discordant for both antibiotic exposure and asthma.